

## AMENDMENTS

### Amendments to the Claims

1. (Previously presented) A modified botulinum neurotoxin type A, wherein the modification comprises ~~comprising at least one or more~~ additional amino acid sequences comprising SEQ ID NO: 27 within the N-terminal 30 amino acids of a light chain from a botulinum toxin type A,

wherein the additional amino acid sequence comprising SEQ ID NO: 27 increases biological-persistence half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional amino acid sequence comprising SEQ ID NO: 27.

2-44 (Canceled)

45. (Currently amended) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of ~~at least one or more~~ additional leucine-based motifs of SEQ ID NO: 17 within the C-terminal 50 amino acids of the light chain, ~~the additional leucine-based motif comprising:~~

- a. ~~a quintet comprising the first five amino acids wherein at least one amino acid is an acidic amino acid or at least one amino acid is a hydroxyl-containing amino acid; and~~
- b. ~~a duplet comprising two amino acids following the quintet wherein at least one of the amino acids is a leucine or at least one of the amino acids is an isoleucine; and~~

wherein the additional leucine-based motif of SEQ ID NO: 17 increases biological persistence half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

46. (Currently amended) The modified botulinum neurotoxin type A of ~~Claim 48~~ Claim 45, wherein the ~~acidic amino acid is selected from the group consisting of a glutamate, a glutamine and an aspartate~~ additional leucine-based motif is SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 10, or SEQ ID NO: 12.
47. (Currently amended) The modified botulinum neurotoxin type A of ~~Claim 48~~ Claim 1, wherein the ~~hydroxyl-containing amino acid is selected from the group consisting of a serine, a threonine and a tyrosine~~ further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 18 within the C-terminal 50 amino acids of the light chain,
- wherein the additional leucine-based motif of SEQ ID NO: 18 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.
48. (Currently amended) The modified botulinum neurotoxin type A of ~~Claim 48~~ Claim 47, wherein the ~~hydroxyl-containing amino acid can be phosphorylated~~ additional leucine-based motif is SEQ ID NO: 1, SEQ ID NO: 4, SEQ ID NO: 6, or SEQ ID NO: 13.
49. (Currently amended) The modified botulinum neurotoxin type A of ~~Claim 48~~ Claim 1, wherein ~~one amino acid of the duplet comprises a leucine, an isoleucine, a methionine, an alanine, a phenylalanine, a tryptophan or a valine~~ further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 22 within the C-terminal 50 amino acids of the light chain,
- wherein the additional leucine-based motif of SEQ ID NO: 22 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.
50. (Currently amended) The modified botulinum neurotoxin type A of ~~Claim 48~~ Claim 49, wherein the ~~duplet comprises a leucine-leucine duplet, a leucine-isoleucine duplet, an~~

~~isoleucine-leucine duplet, an isoleucine-isoleucine duplet or a leucine-methionine duplet~~  
additional leucine-based motif is SEQ ID NO: 2 or SEQ ID NO: 3.

51. (Currently amended) The modified botulinum toxin type A of Claim 1, further comprising a modification of at least one or more additional tyrosine-based motifs of SEQ ID NO: 24 within the C-terminal 50 amino acids of the light chain, ~~the additional tyrosine-based motif comprising four amino acids wherein the amino-terminal amino acid is a tyrosine,~~

wherein the additional tyrosine-based motif of SEQ ID NO: 24 increases biological persistence half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional tyrosine-based motif.

52. (Canceled)

53. (New) The modified botulinum neurotoxin type A of Claim 51, wherein the hydrophobic amino acid of SEQ ID NO: 24 is an alanine, an isoleucine, a leucine, a methionine, a phenylalanine, a tryptophan, a tyrosine, or a valine.

54. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 19 within the C-terminal 50 amino acids of the light chain,

wherein the additional leucine-based motif of SEQ ID NO: 19 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

55. (New) The modified botulinum neurotoxin type A of Claim 54, wherein the additional leucine-based motif is SEQ ID NO: 8.

56. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 20 within the C-terminal 50 amino acids of the light chain,

wherein the additional leucine-based motif of SEQ ID NO: 20 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

57. (New) The modified botulinum neurotoxin type A of Claim 56, wherein the additional leucine-based motif is SEQ ID NO: 9.

58. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 21 within the C-terminal 50 amino acids of the light chain,

wherein the additional leucine-based motif of SEQ ID NO: 21 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

59. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 23 within the C-terminal 50 amino acids of the light chain,

wherein the additional leucine-based motif of SEQ ID NO: 23 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

60. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising a modification of one or more additional leucine-based motifs of SEQ ID NO: 11 within the C-terminal 50 amino acids of the light chain,

wherein the additional leucine-based motif of SEQ ID NO: 11 increases biological half-life of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.